- C. Fabret, S. Poncet, S. Danielsen, T. V. Borchert, S. Dusko Ehrlich and L. Janniere (2000) Efficient gene targeted random mutagenesis in genetically stable Eschericia coli strains. Nucleic Acids Research, 2000, 28:no 21 e95.
- H.-J. Deussen, S. Danielsen, J. Breinholt, and T.V. Borchert (2000) Design and Synthesis of Triglyceride Analogue Biotinylated Suicide Inhibitor for Directed Molecular Evolution of Lipolytic Enzymes. Bioorganic and Medicinal Chemistry Letters 10: 2027-2031.

Andrej M. Brzozowski, David M. Lawson, Johan P. Turkenburg, Henrik Bisgaard-Frantzen, Alan Svendsen, Torben V. Borchert, Zbigniew Dauter, Keith S. Wilson, and Gideon J. Davies (2000) Structural Analysis of a Chimeric Bacterial alpha-amylase. High Resolution Analysis of Native and Ligand Complexes. Biochemistry 39: 9099-9107.

Lars Beier, Allan Svendsen, Carsten Andersen, Torben P. Frandsen, Torben V. Borchert and Joel R. Cherry (2000) Conversion of the maltogenic alpha-amylase into a CGT ase. Protein Engineering 13: 509-513.

H.-J. Deussen, S. Danielsen, J. Breinholt, and T.V. Borchert (2000) A novel Biotinylated Suicide Inhibitor for Directed Molecular Evolution of Lipolytic Enzymes. Bioorganic and Medicinal Chemistry 8: 507-513.

Daniel Legendre, Nezha Laraki, Torbjörn Gräslund, Mads E. Bjørnvad, Michèle Bouchet, Per-Åke Nygren, Torben V. Borchert and Jacques Fastrez (2000) Display of Active Subtilisin 309 on Phage: Analysis of Parameters Influencing the Selection of Subtilisin Variants with Changed Substrate Specificity from Libraries using Phosphonylating Inhibitors. J. Mol. Biol. 296: 87-102.

Jon E. Ness, Mark Welsh, Lori Giver, Manuel Bueno, Joel R. Cherry, Torben V. Borchert, Willom P.C. Stemmer, Jeremy Minshull (1999) DNA shuffling of subgenomic sequences of subtilisin. Nature Biotechnology 17:893-896.

Henrik Bisgaard-Frantzen, Allan Svendsen, Barrie Norman, Sven Pedersen, Søren Kjærulff, Helle Outtrup, and Torben V. Borchert (1999) Development of Industrially Important alpha-Amylases. J. Appl. Glycosci 46: 199-206

Jens E. Nielsen, Lars Beier, Daniel Otzen, Torben V. Borchert, Henrik B. Frantzen, Kim V. Andersen, and Allan Svendsen (1999) Electrostatics in the active site of an alphaamylase. Eur. J. Biochem 264: 816-824.

Zbigniew Dauter, Miroslawa Dauter, A. Marek Brzozowski, Søren Christensen, Torben V. Borchert, Lars Beier, Keith S. Wilson, Gideon Davies (1999) X-ray Structure of Novamyl, the Five-Domain "Maltogenic" alpha-amylase from *Bacillus stearothermophilus*: Maltose and Acarbose Complexes at 1.7 Å Resolution. Biochemistry 38: 8385-8392.

- Barrie E. Norman, Sven Pedersen, Henrik Bisgaard-Frantzen, Daniel Otzen, Torben V. Borchert, Allan Svendsen (1997) The development of a new, heat-stable alpha-amylase for calcium-free starch liquefaction. Proceedings from the Detmold conference 1997.
- Gideon J. Davies, Valerie Ducros, Richard J. Lewis, Torben V. Borchert, Martin Schülein (1997) Oligosaccharide specificity of a family 7 endoglucanase: insertion of potential sugar-binding subsites. J. of Biotechnology 57: 91-100.
- Torben V. Borchert, Soron F. Lassen, Allan Svendsen and Henrik B. Frantzen (1995) Oxidation stable amylases for detergents. Progress in Biotechnology 10: 175-179. Elsevier Science.
- P. Markvardsen, S.F. Lassen, T.V. Borchert, and I.G. Clausen (1995) Uracil-USE, an improved method for site-directed mutagenesis on double-stranded plasmid DNA. Biotechniques 18:370-371
- T. V. Borchert, J. Ph. Zeelen, W. Schliebs, M. Callens, W. Minke, R. Jaenicke, and R. K. Wierenga (1995) An interface point-mutation variant of triosephosphate isomerase is compactly folded and monomeric at low protein concentrations. FEBS Letters 367: 315-318.
- Torben V. Borchert, K.V. Radha Kishan, Johan Ph. Zeelen, Wolfgang Schliebs, Nannada Thanki, Ruben Abagyan, Rainer Jaenicke, and Rik K. Wierenga (1995) Three new crystal structures of point mutation variants of monoTIM: conformational flexibility of loop-1, loop-4 and loop-8. Structure 3: 669-679.
- Myra F. Jacobs, Jens Bo Andersen, Torben V. Borchert, and Vesa P. Kontinen (1995) Identification of a Bacillus subtilis secretion mutant using a beta-galactosidase screening procedure. Microbiology 141: 1771-1779.
- Radha Kishan, Johan Ph. Zeelen, Martin E.M. Noble, Torben V. Borchert, Veronique Mainfroid, Karine Goraj, Joseph A. Martial, and Rik K. Wierenga (1994) Modular mutagenesis of a TIM-barrel enzyme: the crystal structure of a chimeric E. coli TIM having the eighth beta/alpha-unit replaced by the equivalent unit of chicken TIM. Protein Engineering 7: 945-951.
- K.V. Radha Kishan, Johan Ph. Zeelen, Martin E.M. Noble, Torben V. Borchert, and Rik K. Wierenga (1994) Comparison of the structures and the crystal contacts of trypanosomal triosephosphate isomerase in four different crystal forms. Protein Science 3: 779-787.
- T.V.Borchert, M. Mathieu, J.Ph.Zeelen, S.A.Courtneidge, R.K.Wierenga (1994) The crystal structure of human CskSH3: structural diversity near the RT-Src and n-Src loop. FEBS letters 341: 79-85.

Torben V. Borchert, Ruben Abagyan, Rainer Jaenicke, and Rik K. Wierenga (1994) Design, creation and characterization of a stable, monomeric triosephosphate isomerase. Proc. Natl. Acad. Sci. 91: 1515-1518.

T.V. Borchert, R.Abagyan, K.V.R.Kishan, J.Ph.Zeelen, and R.K.Wierenga (1993) The crystal structure of an engineered monomeric triosephosphate isomerase, monoTIM: the correct modelling of an eight-residue loop. Structure 1:205-213.

V.Mainfroid, K.Goraj, F.Rentier-Delrue, A.Houbrechts, A.Loiseau, A.-C.Gohimont, M.E.M.Noble, T.V.Borchert, R.K.Wierenga, and J.A.Martial (1993) Replacing the (beta/alpha)-unit 8 of E. coli TIM with its chicken homologue leads to a stable and active hybrid enzyme. Protein Engineering 6: 893-900.

M.Callens, J.V.Roy, J.Ph.Zeelen, T.V.Borchert, D.Nalis, R.K.Wierenga, F.R.Opperdoes (1993) Selective interaction of glycosomal enzymes from Trypanosoma brucei with hydrophobic cyclic hexapeptides. Bioc.Bioph.Rcs.Comm. 195: 667-672.

Borchert, T.V., Pratt, K., Zcelen, J.Ph., Callens, M., Noble, M.E.M., Opperdoes, F.R., Michels, P.A.M., and Wierenga, R.K. (1993) Overexpression of trypanosomal triosephosphate isomerase in Escherichia coli and characterization of a dimer-interface mutant. Eur. J. Biochem. 211: 703-710.

Rik K. Wierenga, Torben V. Borchert, and Martin E.M. Noble (1992) Crytallographic binding studies with triosephosphate isomerases: conformational changes induced by substrate and substrate-analogues. FEBS letters 307: 34-39.

Torben V. Borchert (1991) A genetic approach in the study of protein secretion in Bacillus subtilis. Thesis, The technical University of Denmark.

Vasantha Nagarajan and Torben V. Borchert (1991) Levansucrase -a tool to study protein secretion in Bacillus subtilis. Res. Microbiol. 142: 787-792.

Torben V. Borchert and Vasantha Nagarajan (1991) Effect of signal sequence alterations on export of levansucrase in Bacillus subtilis. J. Bact. 173: 276-282.

Torben V. Borchert and Vasantha Nagarajan (1990) Structure-function studies on the Bacillus amyloliquefaciens levansucrase signal peptide. pp: 171-177, In "Genetics and Biotechnology of Bacilli", volume 3, Academic Press Inc.

Leslie B. Tang, Reijer Lenstra, Torben V. Borchert, and Vasantha Nagarajan (1990) Isolation and characterization of levansucrase-encoding gene from Bacillus amyloliquefaciens. Gene, 96: 89-93.

Editor:

BBA Protein structure and molecular enzymology (2000) Vol. 1543 (2) Special issue on Protein engineering of enzymes. Guest Editors: H. Dalbøge and Torben V. Borchert.

## Issued Patents: US 5,753,460 (amylase variants) US 5,801,043 (amylase variants) US 5,830,837 (amylase variants) US 5,989,169 (amylase variants) US 6,022,724 (amylase mutants) US 6,093,562 (amylase variants) US 6,143,708 (amylase mutants) US 6,159,687 (method for generating recombined polynucleotides) US 6,159,688 (method of producing polynucleotide variants) US 6,165,718 (method for in vivo production of a mutant library in cells) US 6,187,576 ((amylase variants) US 6,204,232 (amylase mutants) US 6,291,165 (shuffling of heterologous DNA sequences) US 6,297,038 (amylase variants) US 6,309,871 (alkaline amylases) US 6,326,206 (in vivo recombination) US 6,361,989 (amylases) US 6,368,805 (directed recombination) US 6,436,888 (amylases) US 6,440,716 (amylases) US 6,518,042 (diversity generation) US 6,528,298 (amylases)

US 6,541,207 (recombination method)

# **EXHIBIT I**

	Application No.	Applicant(s)
Notice of Allowability	10/025,648	BISGARD-FRANTZEN ET AL.
	Examiner	Art Unit
	Rebecca E. Prouty	1652
The MAILING DATE of this communication apperature All claims being allowable, PROSECUTION ON THE MERITS IS herewith (or previously mailed), a Notice of Allowance (PTOL-85) NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RI of the Office or upon petition by the applicant. See 37 CFR 1.313	(OR REMAINS) CLOSED in this app or other appropriate communication GHTS. This application is subject to	clication. If not included
1. A This communication is responsive to the amendment and c	declaration filed 9/7/04.	
2. The allowed claim(s) is/are <u>48-52</u> .		·
3. A The drawings filed on 19 December 2001 are accepted by the Examiner.		
4. ☑ Acknowledgment is made of a claim for foreign priority un a) ☐ All b) ☐ Some* c) ☒ None of the:  1. ☒ Certified copies of the priority documents have  2. ☐ Certified copies of the priority documents have	been received.	
2. Certified copies of the priority documents have been received in Application No		
<ol> <li>Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).</li> </ol>		
* Certified copies not received:		
Applicant has THREE MONTHS FROM THE "MAILING DATE" of noted below. Failure to timely comply will result in ABANDONMI THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.	of this communication to file a reply of ENT of this application.	complying with the requirements
5. A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.		
6. $\square$ CORRECTED DRAWINGS ( as "replacement sheets") must		
(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached		
1) 🗌 hereto or 2) 🔲 to Paper No./Mail Date		
(b) ☐ including changes required by the attached Examiner's Paper No./Mail Date	Amendment / Comment or in the Of	fice action of
Identifying indicia such as the application number (see 37 CFR 1.8 each sheet. Replacement sheet(s) should be labeled as such in th	34(c)) should be written on the drawing e header according to 37 CFR 1.121(d	gs in the front (not the back) of
7. DEPOSIT OF and/or INFORMATION about the depos attached Examiner's comment regarding REQUIREMENT F	it of BIOLOGICAL MATERIAL m	ust he submitted. Note the
Attachment(s)		
<ol> <li>Notice of References Cited (PTO-892)</li> <li>Notice of Draftperson's Patent Drawing Review (PTO-948)</li> </ol>		tent Application (PTO-152)
•	<ol> <li>Interview Summary ( Paper No./Mail Date</li> </ol>	
<ol> <li>Information Disclosure Statements (PTO-1449 or PTO/SB/08 Paper No./Mail Date</li> </ol>	7. Examiner's Amendm	ent/Comment
4. Examiner's Comment Regarding Requirement for Deposit		nt of Reasons for Allowance
of Biological Material	9. 🗌 Other	
		•

Application/Control Number: 10/025,648 Page 2
Art Unit: 1652

The following is an examiner's statement of reasons for allowance: While claims 48 and 50-52 would appear to be prima facie obvious over Suzuki et al. (JBC 260:6518, 1989) in view of Bisgard-Frantzen et al. (WO95/10603) as explained in the rejection of previous claims 30-33, 35 and 37-39 in the Office Action mailed, 7/29/03, the declaration of Dr. Torben Borchert submitted 9/7/04 establishes that the claimed variants exhibit unexpectedly large increases in thermostability when compared to the increases in thermostability obtained for the corresponding mutations taught by Suzuki et al. As such the claimed variants are non-obvious over the prior art.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Application/Control Number: 10/025,648

Art Unit: 1652

Page 3

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Rebecca Prouty Primary Examiner Art Unit 1652

# **CERTIFICATE OF SERVICE**

I, Richard H. Morse, hereby certify that on June 22, 2005, I caused to be electronically filed a true and correct copy of the foregoing document with the Clerk of the Court using CM/ECF, which will send notification that such filing is available for viewing and downloading to the following counsel of record:

> Donald E. Reid, Esquire Jason Cincilla, Esquire Morris Nichols Arsht & Tunnell 1201 North Market Street PO Box 1347 Wilmington, DE 19899-1347

I further certify that on June 23, 2005, I caused a copy of the foregoing document to be served by hand delivery on the above-listed counsel of record and on the following nonregistered participants in the manner indicated:

#### BY FEDERAL EXPRESS

Kenneth Adamo, Esquire Thomas Friebel, Esquire Tharan, Lanier, Esquire JONES DAY 2882 Sand Hill Road, Suite 240 Menlo Park, CA 94025

> YOUNG CONAWAY STARGATT & TAYLOR, LLP

Richard H. Morse (# 531) Josy W. Ingersoll (# 1088) Karen E. Keller (# 4489)

The Brandywine Building 1000 West Street, 17th Floor

Wilmington, DE 19801 (302) 571-6600

rmorse@ycst.com

Attorneys for Novozymes A/S

### **CERTIFICATE OF SERVICE**

I. Karen E. Keller, hereby certify that on June 29, 2005, I caused to be electronically filed a true and correct copy of the foregoing document with the Clerk of the Court using CM/ECF, which will send notification that such filing is available for viewing and downloading to the following counsel of record:

> Donald E. Reid, Esquire Jason Cincilla, Esquire Morris Nichols Arsht & Tunnell 1201 North Market Street PO Box 1347 Wilmington, DE 19899-1347

I further certify that on June 29, 2005, I caused a copy of the foregoing document to be served by hand delivery on the above-listed counsel of record and on the following nonregistered participants in the manner indicated:

#### BY FEDERAL EXPRESS

Kenneth Adamo, Esquire Thomas Friebel, Esquire Tharan Lanier, Esquire JONES DAY 2882 Sand Hill Road, Suite 240 Menlo Park, CA 94025

YOUNG CONAWAY

STARGATT & TAYLOR, LLP

Richard H. Morse (# 531)

Josy W. Ingersoll (# 1088)

Karen E. Keller (# 4489)

The Brandywine Building

1000 West Street, 17th Floor

Wilmington, DE 19801

(302) 571-6600

kkeller@ycst.com

Attorneys for Novozymes A/S

064080.1001 WP3:1116551.1